observed. This confirmed that the interaction between the capture protein and the ligand was indeed attributable to the BH-3 domain. The same type of experiment was carried out using a small molecule that has been identified as specifically enhancing BH3 protein-protein interaction, and enhancement in ligand (Bcl-XL) binding by a capture molecule (Bak peptide) was observed as expected.

[0171] These experiments were then repeated using several peptides of the BH3 family as ligands to compete with three drugs known to affect Bcl-2 family member function at various concentrations. Bcl-XL was printed on BSA-NHS glass slides as capture proteins in each case. The detected fluorescence of the labeled ligand captured on the slide were shown in columns in **FIGS. 7A and 7B**, different drugs showed differential specificity for the two ligands from the same family. For Bak **(FIG. 7A)**, inhibitory effects were seen in virtually all the cases, while for Bid **(FIG. 7B)**, PNAS or a relatively low concentration of anitmycin does not seem to inhibit its binding. This experiment can be useful in mapping out a drug candidate's specificity regarding each member of a large family of target proteins.

[0172] (iv) Cell Surface Protein Expression

[0173] Monoclonal and scFv antibodies were printed on glass microarrays for detection of cell surface antigen expression in cancer cell lines. Antibodies to c-ErbB2, EGFR, and transferrin receptor were printed on BSA-NHS activated glass slides. With the monoclonal antibodies, less than 2 ng/mL of recombinant antigen labeled with fluorescent dye was detected. For antigen detection in cell extracts, the cell surfaces of cancer cell lines were labeled with fluorescence using NHS-based dyes. This allowed the detection of differential cell surface expression of cErbB2 and EGFR on several cancer cell lines. The transferrin receptor was not detected using the direct labeling approach; however, when a micro-sandwich approach was employed, also the transferrin receptor was detected.

[0174] Monoclonal antibodies to c-ErbB2, EGFR, and transferrin receptor (TfR) were arrayed on a GMS 417 arrayer. The antibodies were spotted in 40% glycerol to prevent drying out of the spots onto BSA-NHS slides. Antibodies were allowed to react with the slide overnight in the cold. The resulting spot size was about 150 micrometer with a spacing of 375 micrometer (center to center).

[0175] Slides were blocked for 30 minutes in 0.5 M glycine and then in BSA for another 30 minutes before samples were added. When multiple samples were processed on a single slide, groups of antibody spots were separated by drawing with a hydrophobic pen to allow up to 24 samples to be processed per slide. Alternatively, the groups of antibody spots were separated using an adhesive Teflon mask allowing 50 or more samples to be processed per slide.

[0176] The samples were usually labeled with Cy3 or Cy5-NHS dyes for one hour at room temperature and un-reacted dye is removed by gel filtration. The cell lines used in this study were the breast adenocarcinoma cell line SKBR3 and the epidermoid carcinoma cell line A-431. Cell surfaces were labeled using the dye, fluorescein-PEG2000-NHS (Shearwater), at 10 mg/mL in PBS for two hours on ice and un-reacted dye was removed by washing the cells before solubilizing in 0.25% SDS in TBS. Recombinant protein antigens were incubated in 2% BSA in 0.1% tween-PBS. Cell lysates were incubated in the lyses buffer without BSA. Following incubation with the samples for two to three hours, the slides were washed 4×10 times: 20 times in TPBS, then 20 times in PBS, by rapid submersion in a beaker containing the wash buffer. The fluorescence was detected using the ArrayWoRx slide reader.

[0177] Sensitivity:

[0178] Microarrays were incubated with serial dilutions of ErbB2 labeled with alexa488 and EGFR labeled with Cy5. After washing, the slide was scanned on the ArrayWoRx. As shown in **FIG. 8**, except for TfR antibody #3, all the antibodies were able to capture ErbB2, TfR, and EGFR respectively. Protein capture was detected at a dilution as low as 1.6 ng/mL.

[0179] Detection of Cell Surface Antigens:

[0180] The breast adenocarcinoma cell line SKBR3, and the epidermoid carcinoma cell line A-431, were grown to confluence and the cell surface labeled with the dye fluorescein-PEG2000NHS. Following labeling, un-reacted dye was removed by washing the cells and the cells were lysed in 0.25% SDS. Total labeled protein (corresponding to about 50,000 cells) was then incubated on the antibody microarray for two hours and the slides scanned on the ArrayWoRx. As shown in **FIG. 9**, the A-431 cell line over-expresses EGFR, but not ErbB2; and the SK-BR-3 cell line over-expresses ErbB2, but only expresses low levels of EGFR. This differential expression of the two receptors in the two cell lines is confirmed by by flow cytometry (e.g., $>10^6$ EGFR receptors per cell in A-431 cells).

[0181] In a different approach, the cell proteins were not labeled directly with fluorescence. Instead, instead, antigen binding to the array was detected with a second fluorescent-labeled antibody to the antigen. The sensitivity of this "sandwich" detection approach was similar to what was observed for the directly labeled recombinant antigens.

[0182] In one experiment, antibodies were printed as before in microarrays and incubated with unlabeled antigens for two hours. Binding was detected with a second antibody to the antigen labeled with Cy5 (for detecting EGFR) or Cy3 (for detecting TfR). Results are shown in **FIG. 10**: monoclonal antibodies as listed in the legend exhibits good sensitivity at about 25 ng/mL.

[0183] The same sandwich approach was performed using phage displayed antibody such as scFv F5 labeled with Cy5.

[0184] For detection of antigens in cell extracts, cell lines (A431 or SKBR-3) were lysed in 0.25% SDS and extracts were incubated with the antibody array for two hours. After washing, bound antigen was detected with fluorescent monoclonal antibodies (for EGFR and TfR) or phage antibody (for ErbB2). As shown in **FIG. 11**, using the sandwich approach, all three antigens, EGFR, ErbB2, or TfR, were detected in both cell lysates. The anti-EGFR antibodies detected the differential expression of ErbB2 in the A431 and SK-BR-3 cell lines (>10 fold difference). Like wise, the anti-ErbB2 phage antibody detected the difference in expression of ErbB2 in the two cell lines. As expected, in the case of transferrin receptor expression, no major difference in expression was detected between the two cell lines.